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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
NIEBAUER, RONALD T	
ART UNIT	PAPER NUMBER
1654	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/716,293	MASSIA ET AL.	
	Examiner	Art Unit	
	RONALD T. NIEBAUER	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 September 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *102,105 and 106* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *102,105-106* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants amendments and arguments filed 9/9/09 are acknowledged and have been fully considered. Any rejection and/or objection not specifically addressed is herein withdrawn. It is noted that the submission of the new ADS (application data sheet) along with the arguments have overcome the 102a rejection.

The original restriction requirement was sent out 7/3/06. On 3/12/07 (as noted in the office action dated 1/7/08) applicants elected group I and the species of SEQ ID NO:124.

In the instant case, the prior art obviate the elected species. In accord with section 803.02 of the MPEP the claims have been examined fully with respect to the elected species.

Claims 1-101,103-104 have been cancelled.

Claims 102,105-106 are under consideration.

Claim Rejections - 35 USC § 103

Claims 102,105-106 were previously rejected under 103 based on the references cited below. The rejection is maintained.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 102,105-106 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rieu et al (Journal Cell Biology 1994 v127 pages 2081-2091 as cited in IDS 11/10/04) and Laplantine et al (Journal of Cell Science 2000 v113 pages 1167-1176; first cited with office action 5/11/09).

Rieu teach that the A-domain of beta2 integrin CR3 is a receptor for the hookworm-derived neutrophil adhesion inhibitor NIF (abstract). Rieu teach that integrins contain binding sites for protein ligands that play essential roles in leukocyte trafficking for example (abstract). Rieu map the NIF binding site to the A-domain and to specific peptide regions (abstract). Rieu teach (page 2086,2089) that the A-domain protein (i.e. r11bA) was immobilized and particular peptides were tested for their ability to inhibit NIF binding. One of the peptides tested (A7 figure 6) corresponded to residues 232-245 and had the amino acid sequence NAFKILVVITDGEK. Rieu teach that the binding site comprised primarily peptide A7 (page 2089 first sentence of first complete paragraph, Figure 6).

Rieu does not expressly teach a peptide of SEQ ID NO:124

Rieu does teach that identification of the region in NIF mediating A-domain binding should be useful to understanding physiological functions (abstract). Rieu teach that the A-domain may be useful for treating hookworm infections (page 2090). Rieu also notes that certain peptides did not absorb adequately (page 2086 first paragraph last sentence). Thus one would be motivated to further study the A-domain NIF interaction.

Laplantine also teach about interactions between integrins and other proteins (title, abstract). Like Rieu, Laplantine recognize that integrins play an important role in triggering intracellular signaling (page 1167, page 1174). Laplantine investigate the interactions between a beta1 integrin and an alpha3 integrin (abstract). Laplantine specifically use surface plasmon resonance to investigate the interaction (page 11169 section 'surface Plasmon resonance, pages 1172-1173, Figure 7). Specifically, Laplantine teach that peptides corresponding to the beta1 subunit and containing an additional N-terminal cysteine residue were immobilized on a dextran through thiol coupling (page 1173 first column). The immobilized peptides were then exposed to peptides corresponding to alpha subunits and binding profiles were recorded (page 1173 first column).

Since Rieu teach investigating the interaction between an integrin and a possible interacting partner one would be motivated to use known techniques that are used to investigate such interactions. Since Rieu teach that identification of the region in NIF mediating A-domain binding should be useful to understanding physiological functions (abstract) and that the A-domain may be useful for treating hookworm infections (page 2090) and that certain peptides did not absorb adequately (page 2086 first paragraph last sentence) one would be motivated to further study the A-domain NIF interaction. Since Laplantine teach surface plasmon resonance

as a specific method to investigate integrin interactions one would be motivated to use the method of Laplantine. Since Laplantine provide a specific example (see Figure 7) one would have a reasonable expectation of success.

Since Rieu teach that the binding site comprised primarily peptide A7 (i.e. NAFKILVVITDGEK) (page 2089 first sentence of first complete paragraph, Figure 6) one would be motivated to use such peptide as the sequence to attach to the dextran. Since Laplantine teach that the dextran is attached via thiol coupling to an additional N-terminal cysteine residue (page 1173 first column) one would be motivated to add an N-terminal cysteine to peptide A7 of Rieu to obtain CNAFKILVVITDGEK and then couple the dextran. The resulting product would be the peptide CNAFKILVVITDGEK (which is SEQ ID NO:124 of the instant invention) covalently attached by thiol coupling to a dextran thus meeting the limitations of claims 102,105-106 of the instant invention.

In the instant case, both Rieu and Laplantine are drawn to methods of identifying interacting regions between integrins and interaction partners. Rieu teach a method in which peptides were adsorbed to plastic wells but notes that numerous peptides did not absorb adequately (page 2086 first paragraph). Laplantine teach a method in which selected peptides containing an additional N-terminal cysteine were immobilized on dextran through thiol coupling and used as part of a surface plasmon resonance analysis. The claims would have been obvious because a particular known technique (i.e. surface plasmon resonance) was recognized as part of the ordinary capabilities of one skilled in the art. From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie*

obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Response to Arguments 103 rejection

Applicants argue (pages 5-7) that the mere binding of a peptide to dextran does not teach a therapeutic conjugate.

Applicants argue that Laplantine teaches the beta1 subunit which is distinguishable from the beta2 subunit.

Applicants argue that the claimed peptide is not suggested from other peptides. Applicants argue that Rieu teach away because Rieu teach a broad interactive region.

Applicants argue that Rieu does not suggest a peptide conjugated to a hydrophilic polymer.

Applicants argue that Laplantine teach coupling to a dextran or an alternative approach.

Applicants argue that a different glycidyl methacrylate approach is used by applicants.

Applicants argue that figure 7 of Laplantine does not teach the instant invention and teaches away by teaching fast dissociation.

Applicants argue that Laplantine does not teach beta2 and is different from Laplantine and one would not be motivated to combine the works.

Applicant's arguments filed 9/9/09 have been fully considered but they are not persuasive.

Although Applicants argue (pages 5-7) that the mere binding of a peptide to dextran does not teach a therapeutic conjugate, it is noted that Laplantine expressly teach that peptides were

'covalently attached by thiol coupling' to a dextran (page 1169 section 'surface Plasmon resonance'). Thus, Laplantine does not teach 'mere binding' as asserted by the applicant. Further, as discussed above the prior art obviate the components of the instant claims, thus there is a reasonable basis that the conjugate is therapeutic. There is no specific definition in the specification to lead one to exclude the conjugate obviated by the prior art. In fact, Rieu teach that the A-domain may be useful for treating hookworm infections (page 2090).

Although Applicants argue that Laplantine teaches the beta1 subunit which is distinguishable from the beta2 subunit, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In the instant case, the rejection is a multiple reference 103 rejection as such any single reference does not expressly teach all of the claim limitations. In the instant case, Rieu teach investigating regions of beta2. Rieu teach (page 2086,2089) that the A-domain protein (i.e. r11bA) was immobilized and particular peptides were tested for their ability to inhibit NIF binding. Thus Rieu recognize a goal of mapping of the binding site (see page 2086 2nd column heading). Rieu also notes direct binding could not be tested for certain peptides since the peptides did not absorb adequately (page 2086 first paragraph last sentence). Since the experiments of Rieu were limited by the inability of certain peptides to bind one would be motivated to use other known methods to test direct binding. As discussed above, Laplantine teach such methods.

Although Applicants argue that the claimed peptide is not suggested from other peptides and that Rieu teach away because Rieu teach a broad interactive region, it is noted that Figure 6

summarizes the work of Rieu. Figure 6a shows that Rieu tested peptides A1,A2,A3,A4,A5,A6,A7,B2,A11,B5,A12. On page (2089 2nd column, first sentence of the last paragraph) Rieu expressly state that A7 is a primary component of the binding domain. Further, Figure 6b shows that A7 inhibits binding better than A1,A2,A3,A4,A5,A6,B2,A11,B5, and A12. Thus, the data and teachings point to the use of A7.

Although Applicants argue that Rieu does not suggest a peptide conjugated to a hydrophilic polymer, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In the instant case, the rejection is a multiple reference 103 rejection as such any single reference does not expressly teach all of the claim limitations. In the instant case, Rieu teach investigating regions of beta2. Rieu teach (page 2086,2089) that the A-domain protein (i.e. r11bA) was immobilized and particular peptides were tested for their ability to inhibit NIF binding. Thus Rieu recognize a goal of mapping of the binding site (see page 2086 2nd column heading). Rieu also notes direct binding could not be tested for certain peptides since the peptides did not absorb adequately (page 2086 first paragraph last sentence). Since the experiments of Rieu were limited by the inability of certain peptides to bind one would be motivated to use other known methods to test direct binding. As discussed above, Laplantine teach such methods.

Although Applicants argue that Laplantine teach coupling to a dextran or an alternative approach, section 2123 II of the MPEP recites that alternative embodiments constitute prior art. In the instant case, Rieu teach investigating regions of beta2. Rieu teach (page 2086,2089) that

the A-domain protein (i.e. r11bA) was immobilized and particular peptides were tested for their ability to inhibit NIF binding. Thus Rieu recognize a goal of mapping of the binding site (see page 2086 2nd column heading). Rieu also notes direct binding could not be tested for certain peptides since the peptides did not absorb adequately (page 2086 first paragraph last sentence). Since the experiments of Rieu were limited by the inability of certain peptides to bind one would be motivated to use other known methods to test direct binding. As discussed above, Laplantine teach such methods, specifically Laplantine expressly teach that peptides were 'covalently attached by thiol coupling' to a dextran (page 1169 section 'surface Plasmon resonance').

Although Applicants argue that a different glycidyl methacrylate approach is used by applicants, it is noted that the features upon which applicant relies (i.e., glycidyl methacrylate approach) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). In the instant case, the claims are drawn to products. Even if the claims were recited as product by process claims, section 2113 of the MPEP states that product by process claims are not limited to the manipulations of the recited steps.

Although Applicants argue that figure 7 of Laplantine does not teach the instant invention and teaches away by teaching fast dissociation, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In the instant case, the rejection is a multiple reference 103 rejection as such any single reference does not expressly teach all of the claim limitations. Further, the

rejection is based on Laplantine, not merely figure 7 of Laplantine. Importantly, Laplantine teach that peptides corresponding to the beta1 subunit and containing an additional N-terminal cysteine residue were immobilized on a dextran through thiol coupling (page 1173 first column) and Laplantine teach experiments using such conjugates (figure 7).

Although Applicants argue that Laplantine does not teach beta2 and is different from Laplantine and one would not be motivated to combine the works, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Since Rieu teach investigating the interaction between an integrin and a possible interacting partner one would be motivated to use known techniques that are used to investigate such interactions. Since Rieu teach that identification of the region in NIF mediating A-domain binding should be useful to understanding physiological functions (abstract) and that the A-domain may be useful for treating hookworm infections (page 2090) and that certain peptides did not absorb adequately (page 2086 first paragraph last sentence) one would be motivated to further study the A-domain NIF interaction. Thus one would be motivated to address the problem set forth in Rieu. In fact, section 2143.01 of the MPEP states: "The court found motivation to combine the references to arrive at the claimed invention in the "nature of the problem to be solved" because each reference was directed "to precisely the same problem of underpinning slumping foundations." Id. at 1276, 69 USPQ2d at 1690. The court also rejected the notion that "an express written motivation to combine must appear in prior art references…." Id. at 1276, 69 USPQ2d at

1690." Further, section 2143.03 of the MPEP states: "person of ordinary skill in the art is also a person of ordinary creativity, not an automaton." KSR International Co. v. Teleflex Inc., 550 U.S. ___, ___, 82 USPQ2d 1385, 1397 (2007). "[I]n many cases a person of ordinary skill will be able to fit the teachings of multiple patents together like pieces of a puzzle." Id. Office personnel may also take into account "the inferences and creative steps that a person of ordinary skill in the art would employ." Id. at ___, 82 USPQ2d at 1396."

Related Prior Art

The prior art previously made of record (5/11/09) and not relied upon is considered pertinent to applicant's disclosure:

Arnaout WO 91/19511: Arnout teach SEQ ID NO:50 (comprises NAFKILVVITDGEK) (see claim 5 for example) and carriers for administering the peptides (claim 17).

Bocher et al (Journal of Immunological Methods 1997 v208 pages 191-202). Bocher teach the use of peptide-dextran conjugates compared to the use of peptide adsorbed onto immunoplates (abstract).

Conclusion

Claims 102,105-106 were previously rejected under 103 based on the references cited above. The rejection is maintained.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to RONALD T. NIEBAUER whose telephone number is (571)270-3059. The examiner can normally be reached on Monday-Thursday, 7:30am-5:00pm, alt. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Anish Gupta/
Primary Examiner, Art Unit 1654

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Examiner, Art Unit 1654